PATENT
Docket No. 348022000500

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Tamara Alcaraz

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In the application of:

Henry LAMPARSKI et al.

Serial No.: To Be Assigned

Filing Date: Herewith

For: ADENOVIRUS VECTORS SPECIFIC FOR CELLS EXPRESSING CARCINOEMBRYONIC ANTIGEN AND METHODS OF USE THEREOF

Examiner: To Be Assigned

Group Art Unit: To Be Assigned

PRELIMINARY AMENDMENT

Box Patent Application
Assistant Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to examination on the merits, Applicants respectfully request entry of this Preliminary Amendment for the above-identified patent application before fees are calculated.

AMENDMENTS

In the specification:

At page 1, under "CROSS-REFERENCE TO RELATED APPLICATIONS" please amend the paragraph containing line 13, as follows:

This application is a continuation of U.S. Patent Application Serial No. 09/033,555, filed March 2, 1998, which claims the benefit of U.S. Provisional Patent Application Serial No. 60/039,763, filed on March 3, 1997, all of which are incorporated by reference herein in their entirety.

At page 11, please amend the paragraph containing line 20, as follows:

Figure 2 depicts the nucleotide sequence (SEQ ID NO:25) of the 5' flanking region of CEA (to about +537).

At page 55, please amend the paragraph containing line 16, as follows:

1. **PCR**: Primers were used to amplify the region of clones of CN741 starting upstream of the CEA insert in the E1A region (primer 39.141C: 5' ATT TGT CTA GGG CCG GGA CTT 3' (SEQ ID NO:21)) and downstream at the 3' end of the EIB region (primer 39.141H: 5' CGC GCG CAA AAC CCC TAA ATA AAG 3' (SEQ ID NO:22)) of adenovirus. The amplified fragment is 4249 bp. The following clones tested positive by PCR: 46.130.7.4., 46.130.8.3, 46.130.9.1.1, 46.130.9.2.1, 46.130.9.3.1, and 46.130.9.4.1.

At page 67, please amend the paragraph containing line 15, as follows:

The structure of CN751 was confirmed by two methods. First, primers 37.124.1 (5' gccttaattaaaagcaaacctcacctccg Ad2 28287bp (SEQ ID NO:23)) and 37.124.4 (5' ggcttaattaactgtgaaaggtgggctgc Ad2 29872bp (SEQ ID NO:25)) were used to screen candidate viruses by PCR to detect the presence of the *adp* cassette. CN751 produced an extension

fragment consistent with the expected product (1065bp). Second, CN751 was analyzed by Southern blot. Viral DNA was purified, digested with PacI, SacI, and AccI/XhoI, and probed with a sequence homologous to the ADP coding region. The structure of CN751 matched the expected pattern.

In the drawings:

Please replace the drawing sheets labeled Figure 2 (1 of 11) through Figure 2 (11 of 11) with the drawing sheets labeled Fig. 2A through 2I enclosed herewith.

In the claims:

Please cancel claims 1-32, without prejudice or disclaimer.

Please add new claims 33-39, as follows:

33. (New) A replication-competent adenovirus vector comprising two adenovirus genes, wherein each of said genes is under transcriptional control of separate carcinoembryonic antigen transcription regulatory elements (CEA-TRE) and wherein said CEA-TREs differ in sequence.

34. (New) The adenovirus vector of claim 33 wherein said CEA-TREs are in tandem orientation.

35. (New) The adenovirus vector of claim 33 wherein said CEA-TREs are in divergent orientation.

36. (New) The adenovirus vector of claim 33 wherein at least one CEA-TRE comprises a promoter that comprises a nucleotide sequence within about -402 to about +69 relative to the transcriptional start site of the CEA gene.

37. (New) The adenovirus vector of claim 33 wherein both of said CEA-TREs comprise a promoter that comprises a nucleotide sequence within about -402 to about +69 relative to the transcriptional start site of the CEA gene.

38. (New) A composition comprising the adenovirus vector of claim 33.

39. (New) A host cell transformed with the adenovirus vector of claim 33.

REMARKS

Claims 1-32 were pending in the present application prior to entry of the present amendment. By virtue of this response, claims 1-32 have been cancelled, without prejudice or disclaimer and new claims 33-39 have been added. Accordingly, claims 33-39 are currently under consideration. Amendment and cancellation of certain claims is not to be construed as a dedication to the public of any subject matter of the claims as previously presented.

Support for the new claims can be found throughout the specification as filed.

Concerning the Drawings

The Figure 2 sheets as originally filed omitted two nucleotides at the right side of each row due to an inadvertent error in the copying process. Replacement sheets for this Figure are enclosed.

The information in the replacement sheets does not constitute new matter for the disclosure. One skilled in the art would readily recognize that the nucleotide sequence in the Figure 2 as originally submitted did not accurately represent the upstream sequence of the CEA gene as already known in the art, as nucleotides are in standard practice presented in blocks of 10 nucleotides, and the last blocks in each row of this figure contained only 8 nucleotides. Further, the numbering of the nucleotides in the figure would indicate to one skilled in the art that nucleotides in the last blocks were missing. One of skill in the art would be able to insert the missing nucleotides based on the CEA upstream sequences publicly available through the National Center for Biology Information, Acc. Nos. U17131 and Z21818; and on the references Willcocks et al. (1990) *Genomics* 8:492-500, Richards et al. (1993) *DNA Seq.* 4:185-196, Richards et al. (1995) *Human Gene Ther.* 6:881–893, Hauck et al. (1995) *J. Biol. Chem.* 270:3602–3610, WO/95/14100; Schrewe et al. (1990) *Mol. Cell. Biol.* 10:2738-2748, which are cited, *inter alia*, at page 5, lines 11 to 16, and page 24, lines 15 to 18, and incorporated by reference (page 6, lines 18 to 19). Thus, one skilled in the art would not only be able to

recognize the existence of this error, but would also recognize the appropriate correction. M.P.E.P.§ 2163.07(b).

Entry of the replacement sheets for Figure 2 is respectfully requested.

Concerning Sequence Listing

Applicants respectfully request that the U.S. Patent and Trademark Office use the Computer Readable Form of the Sequence Listing as filed in the parent application, U.S.S.N. 09/033,555 for the present application.

The undersigned hereby states that the paper copy of the Sequence Listing in the present application is identical to the computer readable copy of the Sequence Listing as submitted in the parent application (U.S.S.N. 09/033,555).

Claims Deemed in Condition for Allowance

In the Office Action mailed July 26, 2000 in the parent application U.S.S.N. 09/033,555, the Examiner deemed that then pending claims 38, 39, and 41 would be allowable if rewritten in independent form including all limitations of the base claim. Applicants have rewritten the subject matter of claims 38, 39, and 41 in order to place them in condition for allowance. Additionally, the Examiner deemed that claims 43 and 44 from U.S.S.N 09/033,555 were free of prior art, but rejected them under Section 112, 2nd paragraph. Current claims 36 and 37 now recite nucleotide sequences relative to the transcriptional start site of the CEA gene.

Applicants respectfully request rejoinder of the methods claims to the extent that they incorporate all the limitations of the composition claims.

Applicants respectfully request consideration and entry of the instant amendment to claims.

Attached hereto is a marked up version of the changes made to the claims and specification by the current amendment with additions underlined and deletions bracketed. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

CONCLUSION

In the unlikely event that the transmittal letter is separated from this document and/or the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 348022000501. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: October 23, 2001

By: ______________________

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

ADENOVIRUS VECTORS SPECIFIC FOR CELLS EXPRESSING CARCINOEMBRYONIC ANTIGEN AND METHODS OF USE THEREOF

In the specification:

At page 1, under "CROSS-REFERENCE TO RELATED APPLICATIONS" the paragraph containing line 13 has been amended, as follows:

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Southern blot. Viral DNA was purified, digested with PacI, SacI, and AccI/XhoI, and probed with a sequence homologous to the ADP coding region. The structure of CN751 matched the expected pattern.

In the claims

Claims 1-32 have been cancelled, without prejudice or disclaimer.

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In the drawings

Figure 2 (1 of 11) through Figure 2 (11 of 11) have been replace with the attached substitute drawing sheets labeled Fig. 2A through Fig. 2I.